REMARKS

The Office Action mailed June 14, 2005 has been received and reviewed. Claims 1–6 are pending in the present application. All claims stand rejected. Applicants have amended claims 1 and 3 as previously set forth. Reconsideration of the application in view of the above amendments and the following remarks is respectfully requested.

Information Disclosure Statement

It is stated in the outstanding Office Action that the listing of references in the specification is not a proper information disclosure statement pursuant to 37 C.F.R. § 1.98(b). It is respectfully submitted that all references cited in the specification were properly submitted by way of an Information Disclosure Statement in the parent application hereto (U.S. Application Serial No. 10/002,842). Pursuant to MPEP § 609 I.A.2, a listing of the information has not been resubmitted in the present divisional application. However, applicants intend all such references to be considered with reference to the subject application. If a separate information disclosure statement must be submitted in the present application to ensure such consideration, please advise accordingly.

35 U.S.C. § 112, Second Paragraph, Rejections

Claims 1 and 2 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Particularly, claim 1 stands rejected as vague and indefinite in reciting "total" endogenous lactoferrin. Clarification is requested as to whether "total" is intended to mean all the lactoferrin found in the sample.

Applicants respectfully submit that the term "total" is intended to describe the complete lactoferrin protein and smaller degraded forms that may occur in the gut following protease and acid digestion. Applicants submit that polyclonal antibodies bind all forms of the protein. *See* Specification paragraphs [0023] and [0058].

With regard to claim 2, it is stated in the outstanding Office Action that use of the phrase "within a linear portion" is vague and indefinite. It is stated that "the specification does not provide a standard for ascertaining the requisite degree." *Office Action*, page 3, ¶4B. Applicants respectfully traverse this rejection. Applicants submit that the specification describes how generate a standard curve and determine the linear portion of the standard curve. According to paragraph [0059] of the specification the "[o]ptical densities (OD_{450}) were determined and plotted versus lactoferrin concentration to generate standard curves. The linear portion of the curve was determined by linear regression analysis using the Log-Log method (Microsoft EXCEL, Microsoft R Office). The lowest dilution of specimen that gave an OD_{450} within the linear portion of the curve was used to determine the lactoferrin concentration. The final concentration was obtained by multiplying the concentration by the dilution factor." Applicants submit that the specification provides the standard to a requisite degree that one would be reasonable apprised of the scope of the invention. In view of the above, Applicants request withdrawal of the 35 U.S.C. § 112, second paragraph, rejection of claims 1 and 2.

35 U.S.C. § 102 Rejections

A.) Applicable Authority

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdeggal Brothers v.*

Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ 2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 2 USPQ 2d 1913, 1920 (Fed. Cir. 1989). *See also*, MPEP § 2131.

B. Anticipation Rejections Based on the Sugi reference (Sugi et al., *The American Journal of Gastroenterology*, vol. 91, no. 5, pp. 927–934, 1996)

Claim 6 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Sugi et al., *The American Jorrnal of Gastroenterology*, vol. 91, no. 5, pp. 927–934, 1996 (hereinafter the "Sugi reference"). As the Sugi reference fails to describe, either expressly or inherently, each and every element as set forth in the rejected claim, Applicants respectfully traverse this rejection, as hereinafter set forth.

Independent claim 6, recites a method for monitoring a patient having inflammatory bowel disease. The method of claim 6 comprises obtaining a first fecal sample from the inflammatory bowel disease patient at a first time, determining the concentration of endogenous lactoferrin in the first fecal sample to obtain a first lactoferrin concentration, obtaining a second fecal sample from the inflammatory bowel disease patient at a second time later than the first time, determining the concentration of endogenous lactoferrin in the second sample to obtain a second lactoferrin concentration, and comparing the first lactoferrin concentration to the second lactoferrin concentration to evaluate any differences therebetween.

By way of contrast, the Sugi reference discloses a method for utilizing fecal lactoferrin as a marker for disease activity in a person having inflammatory bowel disease wherein multiple readings of lactoferrin levels (at 0, 12, 24, 48, 72, and 96 hours after storage at various

temperatures) are taken in a single specimen over time as an assessment of protein stability. *See*, *Sugi reference*, p. 928, col. 2 and FIG. 2. The Sugi reference, however, does not describe, either expressly or inherently, a method for monitoring a patient having inflammatory bowel disease which includes obtaining a first fecal sample from a patient at a first time and obtaining a second fecal sample at a second time later from the same patient than the first time, determining the concentration of the first sample and the second sample and comparing the first lactoferrin concentration to the second lactoferrin concentration to evaluate any differences therebetween as recited in the method of independent claim 6. Rather, the method of the Sugi reference describes two methods. The first method taught by Sugi includes first reading of fecal sample is taken at a first time and a second reading of the same fecal sample is taken at a second time later than the first time. The second method taught by Sugi includes taking multiple samples from the same subject however, these samples are viewed independently and are not compared to each other. Sugi clearly states "[t]hirteen of 41 UC patients and 16 of 34 CD patients were hospitalized two or more times, and **each admission was treated as an independent clinical course.**" Sugi, page 928 last line of column 1. The Sugi reference lacks any description, express or inherent, of comparing the lactoferrin concentration of a first and second sample taken from the same patient at different times in order to evaluate any differences between the samples.

As such, it is respectfully submitted that the Sugi reference fails to describe, either expressly or inherently, each and every element of independent claim 6. Accordingly, claim 6 is not anticipated by the Sugi reference and withdrawal of the 35 U.S.C. §102(b) rejection of this claim is requested.

Furthermore, it is stated in the office action that the claims do not require different first and second samples. Applicants submit that claim 6 clearly requires a first and second sample to be taken from the same patient and two different times and request withdrawal of this rejection as to claim 6. Claim 6 is believed to be in condition for allowance and such favorable action is requested.

35 U.S.C. § 103(a) Obviousness Rejections

A.) Applicable Authority

The basic requirements of a *prima facie* case of obviousness are summarized in MPEP §2143 through §2143.03. In order "[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success [in combining the references]. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)." MPEP § 2143. Further, in establishing a *prima facie* case of obviousness, the initial burden is placed on the Examiner. "To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references. *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985)." *Id. See also* MPEP §706.02(j) and §2142.

B.) Obviousness Rejection Based on the Uchida reference (U.S. Patent 5,552,292)

Claims 1–3 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the U.S. Patent 5,552,992 to Uchida et al. (hereinafter the "Uchida reference"). As the Uchida reference fails to teach or suggest all the limitations of the rejected claims, Applicants respectfully traverse this rejection, as hereinafter set forth.

Independent claim 1, as amended herein, recites an assay for determining a concentration of total endogenous lactoferrin. The assay of claim 1 comprises obtaining a human fecal sample and diluting said fecal sample. The diluted sample is contacted with immobilized polyclonal antibodies to endogenous lactoferrin to create a treated sample. The treated sample is contacted with enzyme-linked polyclonal antibodies to create a readable sample and the optical density of said readable sample is determined at 450 nm. A purified lactoferrin standard curve is generated and the linear portion of the standard curve is determined. The optical density of said readable sample is compared to said standard curve to determine the concentration of the diluted sample. It is determined whether the concentration of the diluted sample is within the linear portion of the standard curve and if so the concentration of the total endogenous lactoferrin is determined.

By way of contrast, the Uchida reference discloses a method for diagnosing gastrointestinal tract disorders, particularly colorectal cancer, by measurement of the level of lactoferrin "in feces by immunoassay and by measurement of the level of whole-sized lactoferrin by immunoassay utilizing monoclonal antibody." *Uchida reference* at col. 1, lines 10–19. The Uchida reference does not provide a method for measuring lactoferrin with enough sensitivity to Claim 1, as amended includes determining whether the concentration of a diluted sample is within the linear portion of the standard curve and if so the concentration of the total endogenous

lactoferrin. This allows for the concentration of lactoferrin in the fecal sample to be more accurately measured than if a linear portion of the standard curve is not determined. The Uchida reference neither teaches nor discloses determining the linear portion of a standard curve for purified lactoferrin. Furthermore, the Uchida reference neither teaches nor discloses determining whether the concentration of lactoferrin of a diluted fecal sample falls within the linear portion of the standard curve.

In view of the above, it is respectfully submitted that the Uchida reference fails to teach or suggest all of the limitations of amended independent claim 1 and, thus, a *prima facie* case of obviousness cannot be established for this claim based upon the Uchida reference. *See*, *In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991). As claim 2 depends from independent claim 1, it is respectfully submitted that a *prima facie* case of obviousness based upon the Uchida reference cannot be established for this claim for at least the same reasons as amended independent claim 1. *See*, *In re Fine*, 5 USPQ 2d 1596, 1600 (Fed. Cir. 1988) (a dependent claim is obvious only if the independent claim from which it depends is obvious); *see also*, MPEP § 2143.03. Accordingly, withdrawal of the 35 U.S.C. § 103(a) rejection of claims 1 and 2 is respectfully requested.

Independent claim 3, as amended herein, recites a kit for distinguishing irritable bowel syndrome from inflammatory bowel disease by determining a concentration of total endogenous lactoferrin in a fecal sample from a person to be diagnosed. The kit of amended claim 3 comprises one or more microassay plates, each plate containing immobilized polyclonal antibodies to human lactoferrin, enzyme-linked polyclonal antibody to human lactoferrin, and enzyme substrate for color development and instructions for performing serial dilutions of a fecal sample.

By way of contrast, the Uchida reference discloses a method for diagnosing gastrointestinal tract disorders, particularly colorectal cancer, by measurement of the level of lactoferrin "in feces by immunoassay and by measurement of the level of whole-sized lactoferrin by immunoassay utilizing monoclonal antibody." *Uchida reference* at col. 1, lines 10–19. The Uchida reference discloses that 50 µl of sample is added to 100 µl of 1%BSA and TBS buffer. Applicants respectfully submit that this is a single dilution of the fecal sample. The Uchida reference does not teach nor disclose instructions for performing serial dilutions on a fecal sample. The serial dilutions of a fecal sample, as disclosed in the present application, allow for the concentration of lactoferrin in the fecal sample to be more accurately measured than if the fecal sample is not serially diluted as described in the Uchida reference.

In view of the above, it is respectfully submitted that the Uchida reference fails to teach or suggest all of the limitations of amended independent claim 3 and, thus, a *prima facie* case of obviousness cannot be established for this claim based upon the Uchida reference. *See*, *In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991). Accordingly, withdrawal of the 35 U.S.C. § 103(a) rejection of claim 3 is respectfully requested.

C.) Obviousness Rejection Based on the Uchida reference in view of the Foster reference (U.S. Patent 4,444,879)

Claims 4 and 5 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the Uchida reference in view of U.S. Patent 4,444,879 to Foster et al. (hereinafter the "Foster reference")

It is respectfully submitted that the Uchida reference in view of the Foster reference fails to teach or suggest all of the limitations of amended independent claim 3. Thus, a *prima facie* case of obviousness cannot be established for this claim based upon the asserted combination of

references. *See*, *In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991). Accordingly, a *prima facie* case of obviousness cannot be established for dependent claims 4 and 5 for at least the above-stated reasons. *See*, *In re Fine*, 5 USPQ 2d 1596, 1600 (Fed. Cir. 1988) (a dependent claim is obvious only if the independent claim from which it depends is obvious); *see also*, MPEP § 2143.03. Accordingly, withdrawal of the 35 U.S.C. § 103(a) rejection of claims 4 and 5 is respectfully requested.

Each of claims 4 and 5 is believed to be in condition for allowance and such favorable action is respectfully requested.

CONCLUSION

Each of claims 1–6 is believed to be in condition for allowance, and a timely notice of allowance solicited. Should it be determined that additional issues remain which might be resolved by a telephone conference, the Examiner is respectfully invited to contact Applicant's undersigned attorney.

It is believed that no fee is due in conjunction with the present Amendment. However, if this belief is in error, the Commissioner is hereby authorized to charge any amount required, or credit any overpayment, to Deposit Account No. 19-2112.

Respectfully submitted,

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